

1. A method for identifying an agent that alleviates insulin resistance in a mammal, the method comprising:

contacting a candidate agent with a mammalian histone deacetylase 2 (HDAC2) polypeptide or a mammalian HDAC2 polynucleotide;

5 identifying the candidate agent as an inhibitor of a biological activity of the polypeptide or expression of the polynucleotide; and

determining whether the candidate agent alleviates insulin resistance in a mammal.

10 2. The method of claim 1, wherein the candidate agent is a peptide, peptidomimetic, amino acid, amino acid analog, polynucleotide, polynucleotide analog, nucleotide, or nucleotide analog.

15 3. The method of claim 1, wherein the candidate agent is a hydroxamic acid derivative, cyclic tetrapeptide, benzamide, or butyrate.

4. The method of claim 1, wherein the candidate agent inhibits deacetylase activity of HDAC2.

20 5. The method of claim 1, comprising determining whether the candidate agent is effective in the treatment of type 2 diabetes.

6. A method for identifying an agent that alleviates insulin resistance in a mammal, the method comprising:

25 providing a candidate agent that inhibits a biological activity of a mammalian HDAC2 polypeptide or expression of a mammalian HDAC2 polynucleotide; and

determining whether the candidate agent alleviates insulin resistance in a mammal.

7. The method of claim 6, wherein the candidate agent is a peptide, peptidomimetic, amino acid, amino acid analog, polynucleotide, polynucleotide analog, nucleotide, or nucleotide analog.

5 8. The method of claim 6, wherein the candidate agent is a hydroxamic acid derivative, cyclic tetrapeptide, benzamide, or butyrate.

9. The method of claim 6, wherein the candidate agent inhibits deacetylase activity of HDAC2.

10 10. The method of claim 6, comprising determining whether the candidate agent is effective in the treatment of type 2 diabetes.

11. A method for identifying an agent that alleviates insulin resistance in a mammal, the method comprising:

15 contacting an HDAC2 polypeptide or an insulin receptor substrate 1 (IRS-1) polypeptide with a candidate agent;

 detecting the binding of the candidate agent to the HDAC2 polypeptide or the IRS-1 polypeptide; and

20 determining whether the candidate agent alleviates insulin resistance in a mammal.

12. The method of claim 11, wherein the HDAC2 polypeptide or the IRS-polypeptide is immobilized during the contacting step.

25 13. The method of claim 11, wherein the candidate agent is immobilized during the contacting step.

14. The method of claim 11, wherein the candidate agent is a peptide, peptidomimetic, amino acid, amino acid analog, polynucleotide, polynucleotide analog, nucleotide, or nucleotide analog.

15. The method of claim 11, wherein the contacting step is carried out using an *in vitro* system.

5 16. The method of claim 15, wherein the *in vitro* system is a cell-free system.

17. The method of claim 11, further comprising determining whether the candidate agent is effective in the treatment of type 2 diabetes.

10 18. A method for identifying an agent that increases acetylation of IRS-1, the method comprising:

 contacting a candidate agent with a mammalian IRS-1 polypeptide; and
 determining whether the candidate agent increases acetylation of the IRS-1 polypeptide.

15 19. The method of claim 18, further comprising determining whether the candidate agent is effective in alleviating insulin resistance.

20 20. The method of claim 18, further comprising determining whether the candidate agent is effective in the treatment of type 2 diabetes.

21. A method for alleviating insulin resistance in a mammal, the method comprising administering to a mammal in need thereof an effective amount of an inhibitor of HDAC2.

25 22. The method according to claim 21, wherein the inhibitor of HDAC2 is trichostatin A.

30 23. The method of claim 21, wherein the inhibitor of HDAC2 is a hydroxamic acid derivative, cyclic tetrapeptide, benzamide, or butyrate.

24. The method of claim 21, wherein the inhibitor of HDAC2 inhibits deacetylase activity of HDAC2.

25. The method of claim 21, wherein the mammal is a human.

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26. The method of claim 25, wherein the human has type 2 diabetes.

27. A method for alleviating insulin resistance in a mammal, the method comprising administering to a mammal in need thereof an effective amount of an agent that increases acetylation of IRS-1.

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28. The method of claim 27, wherein the mammal is a human.

29. The method of claim 28, wherein the human has type 2 diabetes.

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